

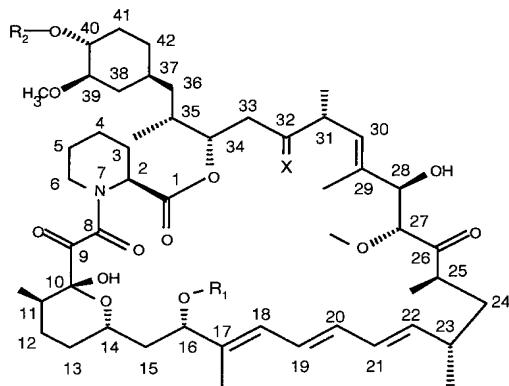
### **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1-3. (Canceled)

Claim 4. (Original) A method for treating abnormally increased bone turnover or resorption in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of a rapamycin derivative of formula I



wherein

$R_1$  is  $CH_3$  or  $C_{3-6}$ alkynyl,

$R_2$  is H or  $-\text{CH}_2\text{-CH}_2\text{-OH}$ , 3-hydroxy-2-(hydroxymethyl)-2-methyl-propanoyl or tetrazolyl, and X is  $=\text{O}$ , (H,H) or (H,OH),

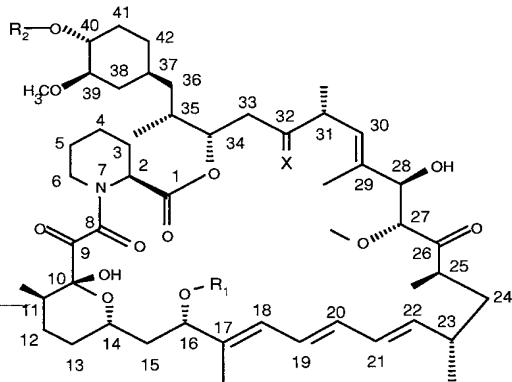
provided that  $R_2$  is other than H when X is =O and  $R_1$  is  $CH_3$ ,

or a prodrug thereof when  $R_2$  is  $-\text{CH}_2\text{-CH}_2\text{-OH}$ , e.g. a physiologically hydrolysable ether thereof.

Claim 5. (Original) A method for treating abnormally increased bone turnover or resorption in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of rapamycin or a rapamycin derivative, concomitantly or sequentially with a second drug selected from bone resorption inhibitor, a calcitonin or an analogue or derivative thereof; a steroid hormone, a partial estrogen agonist or estrogen-gestagen combination; a selective estrogen receptor modulator; vitamin D or an analogue thereof; Parathyroid Hormone (PTH), a PTH fragment or a PTH derivative; a bisphosphonate; a cathepsin K inhibitor; a PTH releaser; a selective androgen receptor molecule; and strontium ranelate.

Claim 6-8. (Cancelled)

Claim 9. (Previously presented) A method for the treatment of osteoporosis; bone loss secondary to or due to medication; bone loss associated with immobilisation and space flight; bone loss associated with rheumatoid arthritis, osteopenia, osteogenesis imperfecta, hyperthyroidism, anorexia nervosa, organ transplantation, joint prosthesis loosening; periarticular bone erosions in rheumatoid arthritis; osteoarthritis; hypercalcemia; bone cancer and bone metastases; and/or multiple myeloma, in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of rapamycin or a rapamycin derivative of formula I



I

wherein

$R_1$  is  $CH_3$  or  $C_{3-6}$ alkynyl,

$R_2$  is H or  $-CH_2-CH_2-OH$ , 3-hydroxy-2-(hydroxymethyl)-2-methyl-propanoyl or tetrazolyl, and X is  $=O$ , (H,H) or (H,OH),

provided that  $R_2$  is other than H when X is  $=O$  and  $R_1$  is  $CH_3$ ,

or a prodrug thereof when  $R_2$  is  $-CH_2-CH_2-OH$ , e.g. a physiologically hydrolysable ether thereof,

concomitantly or sequentially with a second drug selected from bone resorption inhibitor, a calcitonin or an analogue or derivative thereof; a steroid hormone, a partial estrogen agonist or estrogen-gestagen combination; a selective estrogen receptor modulator; vitamin D or an analogue thereof; Parathyroid Hormone (PTH), a PTH fragment or a PTH derivative; a bisphosphonate; a cathepsin K inhibitor; a PTH releaser; a selective androgen receptor molecule; and strontium ranelate.

Claim 10-11. (Canceled)

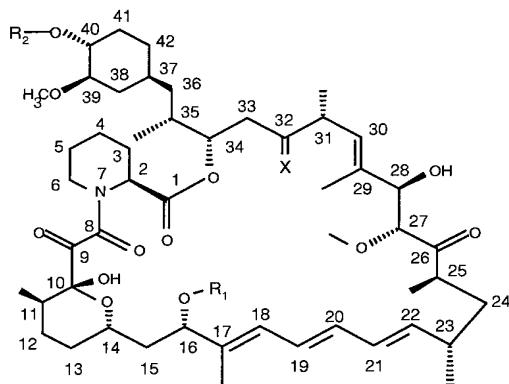
Claim 12. (Previously presented) The method according to claim 4 wherein the rapamycin derivative is selected from 40-O-(2-hydroxyethyl)-rapamycin, 40-[3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate]-rapamycin, 40-epi-(tetrazolyl)-rapamycin, 32-deoxorapamycin, 16-pent-2-ynyl-32(S)-dihydro rapamycin, and TAFA-93.

Claim 13. (Previously presented) The method according to claim 4 wherein the rapamycin derivative is 40-O-(2-hydroxyethyl)-rapamycin.

Claim 14. (Previously presented) The method according to claim 9 wherein the rapamycin derivative is selected from 40-O-(2-hydroxyethyl)-rapamycin, 40-[3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate]-rapamycin, 40-epi-(tetrazolyl)-rapamycin, 32-deoxorapamycin, 16-pent-2-ynyloxy-32(S)-dihydro rapamycin, and TAFA-93.

Claim 15. (Previously presented) The method according to claim 9 wherein the rapamycin derivative is 40-O-(2-hydroxyethyl)-rapamycin.

Claim 16. (Previously presented) The method according to claim 5 wherein the rapamycin derivative is a compound of formula I



wherein

R<sub>1</sub> is CH<sub>3</sub> or C<sub>3-6</sub>alkynyl,

R<sub>2</sub> is H or -CH<sub>2</sub>-CH<sub>2</sub>-OH, 3-hydroxy-2-(hydroxymethyl)-2-methyl-propanoyl or tetrazolyl, and X is =O, (H,H) or (H,OH),

provided that R<sub>2</sub> is other than H when X is =O and R<sub>1</sub> is CH<sub>3</sub>,

or a prodrug thereof when R<sub>2</sub> is -CH<sub>2</sub>-CH<sub>2</sub>-OH, e.g. a physiologically hydrolysable ether thereof.

Claim 17. (Previously presented) The method according to claim 5 wherein the rapamycin derivative is selected from 40-O-(2-hydroxyethyl)-rapamycin, 40-[3-hydroxy-2-(hydroxymethyl)-2-methylpropanoate]-rapamycin, 40-epi-(tetrazolyl)-rapamycin, 32-deoxorapamycin, 16-pent-2-ynyloxy-32(S)-dihydro rapamycin, and TAFA-93.

Claim 18. (Previously presented) The method according to claim 5 wherein the rapamycin derivative is 40-O-(2-hydroxyethyl)-rapamycin.